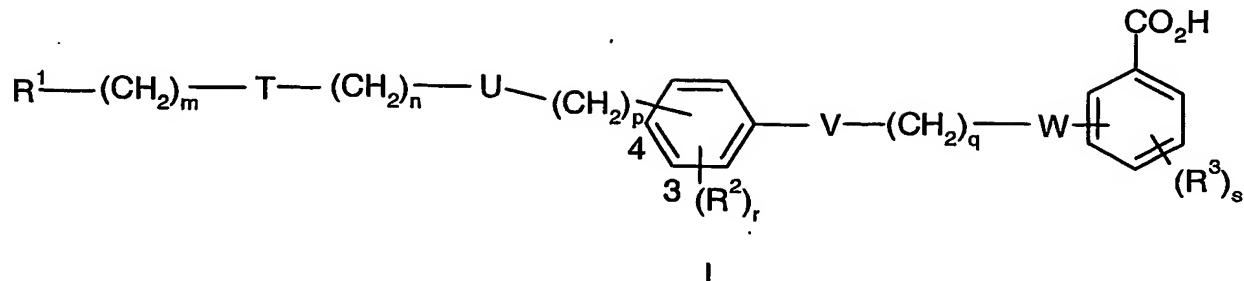


Claims

1. A compound of formula I



5

wherein

R^1 represents aryl optionally substituted by a heterocyclic group or a heterocyclic group optionally substituted by aryl wherein each aryl or heterocyclic group is optionally substituted by one or more of the following groups:

10 a C_{1-6} alkyl group;a C_{1-6} acyl group;

aryl C_{1-6} alkyl, wherein the alkyl, aryl, or alkylaryl group is optionally substituted by one or more R^b ;

halogen,

15 -CN and NO_2 ,- NR^cCOOR^a ;- NR^cCOR^a ;- NR^cR^a ;- $NR^cSO_2R^d$;20 - $NR^cCONR^kR^c$;- $NR^cCSNR^aR^k$;- OR^a ;- OSO_2R^d ;- SO_2R^d ;25 - SOR^d ;- SR^e ;- $SO_2NR^aR^f$;

-SO₂OR^a;

-CONR^cR^a;

-OCONR^fR^a;

wherein R^a represents H, a C₁₋₆alkyl group, aryl or arylC₁₋₆alkyl group wherein the alkyl,

5 aryl or arylC₁₋₆alkyl group is optionally substituted one or more times by R^b, wherein R^b represents C₁₋₆alkyl, aryl, arylC₁₋₆alkyl, cyano, -NR^cR^d, =O, halo, -OH, -SH, -OC₁₋₄alkyl, -Oaryl, -OC₁₋₄alkylaryl, -COR^c, -SR^d, -SOR^d, or -SO₂R^d, wherein R^c represents H, C₁₋₄alkyl, aryl, arylC₁₋₄alkyl and R^d represents C₁₋₄alkyl, aryl, arylC₁₋₄alkyl;

10 wherein R^f represents hydrogen, C₁₋₄alkyl, C₁₋₄acyl, aryl, arylC₁₋₄alkyl and R^a is as defined above; and

R^k represents hydrogen, C₁₋₄alkyl, aryl, arylC₁₋₄alkyl;

the group -(CH₂)_m-T-(CH₂)_n-U-(CH₂)_p- is attached at either the 3 or 4 position in the phenyl ring as indicated by the numbers in formula I and represents a group selected from 15 one or more of the following: O(CH₂)₂, O(CH₂)₃, NC(O)NR⁴(CH₂)₂, CH₂S(O₂)NR⁵(CH₂)₂, CH₂N(R⁶)C(O)CH₂, (CH₂)₂N(R⁶)C(O)(CH₂)₂, C(O)NR⁷CH₂, C(O)NR⁷(CH₂)₂, and CH₂N(R⁶)C(O)CH₂O;

V represents O, S, NR⁸, or a single bond;

20

q represents 1, 2 or 3 ;

W represents O, S, N(R⁹)C(O), NR¹⁰, or a single bond;

25 R² represents halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a C₁₋₄alkoxy group which is optionally substituted by one or more fluoro, a C₁₋₄acyl group, aryl, an arylC₁₋₄alkyl group, CN or NO₂ ;

r represents 0, 1, 2 or 3 ;

30

R³ represents represents halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a C₁₋₄alkoxy group which is optionally substituted by one or more fluoro, a C₁₋₄acyl group, aryl, an arylC₁₋₄alkyl group, or CN ;

5 s represents 0, 1, 2 or 3 ; and

R⁴, R⁵, R⁶, R⁷, R⁸, R⁹ and R¹⁰ independently represent H, a C₁₋₁₀alkyl group, aryl or an arylC₁₋₄alkyl group or when m is 0 and T represents a group N(R⁶)C(O) or a group (R⁵)NS(O₂) then R¹ and R⁶ or R¹and R⁵ together with the nitrogen atom to which they are

10 attached represent a heteroaryl group;

and pharmaceutically acceptable salts thereof ;

with the provisos that when

1) when R¹ is phenyl optionally substituted by one or two groups independently selected from halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a

15 C₁₋₄alkoxy group which is optionally substituted by one or more fluoro;

m is 1;

T is N(R⁶)C(O) wherein R⁶ represents a C₂₋₈alkyl group which is optionally interrupted by oxygen;

n is 1;

20 U is absent or represents methylene;

p is 0;

r is 0;

V is O or S;

q is 1; and

25 W is a single bond attached to the position ortho to the carboxylic acid group;

then s does not represent 0; and

2) when R¹ is phenyl optionally substituted by one or two groups independently selected from halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a

30 C₁₋₄alkoxy group which is optionally substituted by one or more fluoro;

m is 1;

T is N(R⁶)C(O) wherein R⁶ represents an unbranched C₂₋₇alkyl group;

n is 1;

U is O;

p is 0;

r is 0 or 1;

5 and when r is 1 R² is attached at the 3 position and is OCH₃;

V is a single bond;

q is 2; and

W is O or S attached to the position ortho to the carboxylic acid group;

then s does not represent 0.

10

2. A compound according to claim 1 in which R¹ represents phenyl which is optionally substituted by one or more of the following: halo, hydroxy, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a C₁₋₄alkoxy group which is optionally substituted by one or more fluoro, benzyloxy, a C₁₋₄alkylsulphonyloxy group, phenyl or a heteroaryl group, or R¹ represents heteroaryl which is optionally substituted by one or more of the following: halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a C₁₋₄alkoxy group which is optionally substituted by one or more fluoro or phenyl optionally substituted by one or more of the following: halo, a C₁₋₄alkyl group which is optionally substituted by one or more fluoro, a C₁₋₄alkoxy group which is optionally substituted by one or more fluoro.

15

20

3. A compound according to any previous claim in which the group -(CH₂)_m-T-(CH₂)_n-U-(CH₂)_p- is attached at the 4 position in the phenyl ring as indicated by the numbers in formula I, that is para to the group V.

25

4. A compound according to any previous claim in which the group -V-(CH₂)_q-W- represents a group selected from: OCH₂, SCH₂, NHCH₂, CH₂CH₂S or CH₂CH₂O.

30

5. A compound according to any previous claim in which the group -V-(CH₂)_q-W-

represents the group OCH₂.

6. A compound according to any previous claim in which the group $-V-(CH_2)_q-W-$ is joined at the ortho position with respect to the carboxylic acid group.
7. A compound according to any previous claim in which R^2 is halo, a C_{1-4} alkyl group or a C_{1-4} alkoxy group and r is 0 or 1.
8. A compound according to any previous claim in which s is 0.
9. A compound selected from one or more of the following:
 10. 3-{{[(3-{{[(1,1'-biphenyl-4-ylcarbonyl)amino]methyl}phenyl)amino]methyl}benzoic acid; 2-{{[4-(2-oxo-2-{{[4-(trifluoromethyl)benzyl]amino}ethyl)phenoxy]methyl}benzoic acid; 2-{{[3-{{2-[benzyl(hexyl)amino]-2-oxoethyl}phenoxy)methyl}benzoic acid; 2-{{[3-(2-oxo-2-{{[4-(trifluoromethyl)benzyl]amino}ethyl)phenoxy]methyl}benzoic acid; 2-{{[4-{{3-[2-(3,4-dimethoxyphenyl)ethyl](methyl)amino}-3-oxopropyl}phenoxy}-methyl}benzoic acid;
 15. 2-{{[4-{{2-[(4-methyl-2-[4-(trifluoromethyl)phenyl]-1,3-thiazol-5-yl}carbonyl)amino}-ethyl}phenoxy)methyl}benzoic acid; 2-{{[4-{{2-({[(2,4-difluorophenyl)amino]carbonyl}amino)ethyl}phenoxy}methyl}benzoic acid;
 20. 2-{{[4-{{2-[(2-methyl-5-phenyl-3-furoyl)amino]ethyl}phenoxy}methyl}benzoic acid; 2-{{[4-{{2-[(benzylsulfonyl)amino]ethyl}phenoxy}methyl}benzoic acid; 2-{{[4-{{2-[benzyl(hexyl)amino]-2-oxoethyl}-2-fluorophenoxy)methyl}benzoic acid; 2-{{[4-{{2-[benzyl(hexyl)amino]-2-oxoethyl}-2-methoxyphenoxy)methyl}benzoic acid; 2-{{[4-{{3-(3,4-dihydroisoquinolin-2(1H)-yl)-3-oxopropyl}phenoxy}methyl}benzoic acid;
 25. 2-{{[4-{{2-[(4-(1H-imidazol-1-yl)phenoxy]ethyl}-phenoxy)methyl}benzoic acid; 2-{{[4-{{2-[(methylsulfonyl)oxy]phenoxy}ethyl}phenoxy]methyl}benzoic acid; 2-{{[3-{{2-[(benzyloxy)phenoxy]ethyl}phenoxy}methyl}benzoic acid; 2-{{[3-{{2-[(methylsulfonyl)oxy]phenoxy}ethyl}phenoxy]methyl}benzoic acid;
 30. 2-{{[4-{{3-[(4-(benzyloxy)phenoxy]propyl}phenoxy}methyl}benzoic acid; 2-{{[4-{{3-[(methylsulfonyl)oxy]phenoxy}propyl}phenoxy]methyl}benzoic acid; 2-{{[4-[(4-hydroxyphenoxy)propyl]phenoxy}methyl}benzoic acid;

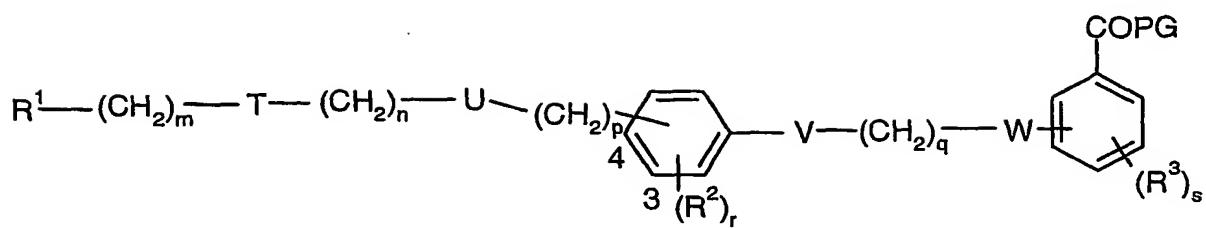
2-{{[4-(3-{{[2-(2-ethoxyphenyl)ethyl]amino}-3-oxopropyl}phenoxy]methyl}benzoic acid; 2-[(4-{3-[ethyl(2-pyridin-2-ylethyl)amino]-3-oxopropyl}phenoxy)methyl]benzoic acid; 2-{{[2-(3-{{2-[benzyl(hexyl)amino]-2-oxoethoxy}phenyl}ethyl]thio}benzoic acid; 2-{{[4-(2-{heptyl[2-(2-methoxyphenyl)ethyl]amino}-2-oxoethyl}phenoxy]methyl}benzoic acid; 2-[(4-{2-[[2-(4-chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl}phenoxy)methyl]benzoic acid; 2-[(4-{2-[heptyl(2-phenylethyl)amino]-2-oxoethyl}-phenoxy)methyl]benzoic acid; 2-[(4-{2-[ethyl(2-fluorobenzyl)amino]-2-oxoethoxy}phenoxy)methyl]benzoic acid; 10 2-[(4-{2-[ethyl(2-fluorobenzyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid; 2-[(4-{2-[heptyl(2-phenylethyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid; 2-{2-[4-(2-{isobutyl[4-(trifluoromethyl)benzyl]amino}-2-oxoethoxy)phenyl]ethoxy}-benzoic acid; and 15 2-[(4-{2-[[2-(4-chlorophenyl)ethyl](heptyl)amino]-2-oxoethyl}benzyl)oxy]benzoic acid and pharmaceutically acceptable salts thereof.

10. A pharmaceutical formulation comprising a compound according to any preceding claim in admixture with pharmaceutically acceptable adjuvants, diluents and/or carriers.

20 11. A method of treating or preventing insulin resistance comprising the administration of a compound according to any one of claims 1 to 9 to a mammal in need thereof.

12. The use of a compound according to any one of claims 1 to 9 in the manufacture of a medicament for the treatment of insulin resistance.

25 13. A process to prepare compounds of formula I comprising reacting a compound of formula II



in which R^1 , T , U , V , W , R^2 , R^3 , m , n , p , q , r and s are as previously defined and PG represents a protecting group for a carboxylic hydroxy group with a de-protecting agent.

5 14. Compounds of formula II as described in claim 13.